

LISTING OF CLAIMS

1. (Original) A packaging construct for regulatable expression of flavivirus structural proteins in an animal cell, said vector comprising a regulatable promoter operably linked to a nucleotide sequence encoding a flavivirus structural protein translation product that comprises C protein, prM protein and E protein.
2. (Original) The packaging construct of claim 1, wherein the regulatable promoter is tetracycline-repressible.
3. (Original) The packaging construct of claim 2 wherein the regulatable promoter is a tetracycline repressible CMV promoter.
4. (Original) The packaging construct of claim 1, wherein the nucleotide sequence encodes one or more variant or mutated flavivirus structural proteins respectively having at least 80% amino acid sequence identity to C protein, prM protein or E protein.
5. (Original) The packaging construct of claim 1, further comprising an IRESNeo selection marker nucleotide sequence.
6. (Original) The packaging construct of claim 1 wherein the C protein, prM protein and E protein are structural proteins of Kunjin virus.
7. (Original) A packaging cell comprising the packaging construct of claim 1.
8. (Original) A packaging cell comprising the packaging construct of claim 2 and a tetracycline transactivator construct.
9. (Original) The packaging cell of claim 7, which is a BHK21 cell.

10. (Original) A flaviviral packaging system comprising: (i) a packaging construct according to claim 1; and (ii) a flaviviral expression construct comprising: (a) a flaviviral replicon; (b) a heterologous nucleic acid; and (c) a promoter operably linked to said replicon.

11. (Original) The flaviviral packaging system of claim 10, wherein the flaviviral replicon is a Kunjin virus replicon, Dengue virus replicon or a West Nile virus replicon.

12. (Original) The flaviviral packaging system of claim 10, wherein the heterologous nucleic acid encodes one or more proteins expressible in an animal cell.

13. (Original) The flaviviral packaging system of claim 12, wherein the one or more proteins is/are immunogenic.

14. (Currently amended) The flaviviral packaging system of Claim ~~11~~¹⁴ wherein the replicon ~~is a Kunjin virus replicon that encodes one or more~~ one or more mutated non-structural proteins selected from the group consisting of:

- (i) Leucine residue 250 substituted by Proline in the NS1 non-structural protein.
- (ii) Alanine 30 substituted by Proline in the nonstructural protein NS2A;
- (iii) Asparagine 101 substituted by Aspartate in the nonstructural protein NS2A; and
- (iv) Proline 270 substituted by Serine in the nonstructural protein NS5.

15. (Canceled)

16. (Original) The flaviviral packaging system of claim 10, wherein the regulatable promoter is tetracycline-repressible.

17. (Original) The flaviviral packaging system of claim 16 wherein the regulatable promoter is a tetracycline repressible CMV promoter.

18. (Original) The flaviviral packaging system of claim 10 wherein the flaviviral expression construct is in RNA form.

19. (Original) A packaging cell comprising the flaviviral packaging system of claim 10.
20. (Original) A packaging cell comprising the flaviviral packaging system of claim 16 and a tetracycline transactivator construct.
21. (Original) The packaging cell of claim 19 or claim 20, which is a BHK21 cell.
22. (Original) A method of producing flavivirus VLPs including the step of: (i) introducing the packaging construct of claim 1 into a host cell to thereby produce a packaging cell; (ii) introducing into said packaging cell a flaviviral expression construct comprising: (a) a flaviviral replicon; (b) a heterologous nucleic acid; and (c) a promoter operably linked to said replicon; and (iii) inducing production of one or more VLPs by said packaging cell.
23. (Original) The method of claim 22, wherein the flaviviral expression construct is in RNA form.
24. (Original) Flaviviral VLPs produced according to the method of claim 22.
25. (Currently amended) An ~~immunotherapeutic~~ immunogenic composition comprising the VLPs of claim 24 and a pharmaceutically acceptable carrier diluent or excipient.
26. (Canceled)
27. (Withdrawn) A method of producing a recombinant protein including the step of infecting a host cell with the VLPs of claim 24, whereby said heterologous nucleic acid encoding said protein is expressed in said host cell.
28. (Withdrawn) The method of claim 27, wherein the host cell is a mammalian cell.

29. (Withdrawn) A method of immunizing an animal including the step of administering the immunotherapeutic composition of claim 26 to the animal to thereby induce an immune response in the animal.

30. (Withdrawn) The method of claim 29, wherein the animal is a mammal.

31. (Withdrawn) The method of claim 30, wherein the mammal is a human.

32. (Previously presented) A method of immunizing an animal including the steps of:

- (i) introducing the packaging construct of Claim 1 into a host cell to thereby produce a packaging cell;
- (ii) introducing into said packaging cell a flaviviral expression construct comprising:
 - (a) a flaviviral replicon;
 - (b) a heterologous nucleic acid; and
 - (c) a promoter operably linked to said replicon; and
- (iii) inducing production of one or more VLPs by said packaging cell;
- (iv) combining the one or more VLPs with a pharmaceutically acceptable carrier diluent or excipient to form a vaccine; and
- (v) administering the vaccine to the animal to thereby induce an immune response in the animal.

33. (Previously presented) The method of Claim 32, wherein the animal is a mammal.

34. (Previously presented) The method of Claim 33, wherein the mammal is a human.

35. (Previously presented) A method of producing a recombinant protein including the steps of:

- (i) introducing the packaging construct of Claim 1 into a first host cell to thereby produce a packaging cell;
- (ii) introducing into said packaging cell a flaviviral expression construct comprising:
 - (a) a flaviviral replicon;

- (b) a heterologous nucleic acid; and
- (c) a promoter operably linked to said replicon;
- (iii) inducing production of one or more VLPs by said packaging cell;
- (iv) infecting a second host cell with the VLPs produced at step (iii) whereby said heterologous nucleic acid encoding said protein is expressed in said second host cell.

36. (Previously presented) The packaging construct of Claim 1, wherein the regulatable promoter has a promoter activity controllable in response to one or more physical or chemical regulatory agents.

37. (Previously presented) The packaging construct of Claim 1, suitable for stable expression of flavivirus structural proteins.

38. (New) The method of Claim 35, wherein the flaviviral expression construct is in RNA form.

39. (New) The method of Claim 35, wherein the second host cell is a mammalian cell.